inaccessible to them. Therefore, the use of probes of increasing size appears to be a tool for studying not only the lateral, but also the longitudinal distribution of cell surface binding sites. However, since the number of labelled particles bound to a surface is less than that of the free molecules, the gold method does not allow an absolute quantification of specific surface receptors. This restriction also applies to other particulate markers.

Conclusion

While the gold method has found some uses in histochemistry, its main application is in cytochemistry using both SEM and TEM. The method is general and its versatility resides in the wide variety of macromolecules which can be adsorbed onto gold particles. Gold markers can be prepared rapidly and inexpensively, they show little non-specific adsorption and can be quantified by various methods. They are also useful for multiple marking experiments. Finally, using the technique, intracellular antigens can be located on thin sections on which the gold particles can be clearly identified.

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References

1 A. H. Coons, H. J. Creech, R. N. Jones and E. Berliner, *J. Immunol.*, 1942, **45**, 159-170
2 P. K. Nakane and G. B. Pierce, *J. Histochem. Cytochem.*, 1966, **14**, 929-931
3 S. Avrameas, *Bull. Soc. Chim. Biol.*, 1968, **50**, 1169-1178
4 L. A. Sternberger, P. H. Hardy, J. J. Cuculis and H. G. Meyer, *J. Histochem. Cytochem.*, 1970, **18**, 315-333
5 S. J. Singer, *Nature*, 1959, **183**, 1523-1524
6 S. J. Singer and A. F. Schick, *J. Biophys. Biochem. Cytol.*, 1961, **9**, 519-525
7 W. P. Faulk and G. M. Taylor, *Immunochemistry*, 1971, **8**, 1081-1083
8 M. Horisberger, J. Rosset and H. Bauer, *Experientia*, 1975, **31**, 1147-1148
9 M. Horisberger and M. Vonlanthen, *Histochemistry*, 1979, **64**, 115-118
10 L. C. Hoyer, J. C. Lee and C. Bucana, in 'SEM/1979/III', SEM Inc., AMF O'Hare, IL. 60666, pp. 629-636
11 M. Horisberger and J. Rosset, *J. Histochem. Cytochem.*, 1977, **25**, 295-305
12 W. D. Geoghegan and G. A. Ackerman, *J. Histochem. Cytochem.*, 1977, **25**, 1187-1200
13 M. Horisberger, *Biol. Cell.*, 1979, **36**, 253-258
14 S. L. Goodman, G. M. Hodges and D. C. Livingston, in 'SEM/1980/I', SEM Inc., AMF O'Hare, IL. 60666, pp. 136-146
15 M. Horisberger, in 'SEM/1981', SEM Inc., AMF O'Hare, IL. 60666, in press
16 M. Faraday, *Ann. Phys.*, 1857, **101**, 383
17 G. Frens, *Nature Phys. Sci.*, 1973, **241**, 20-22
18 M. Horisberger and M. Vonlanthen, *J. Microsc.*, 1979, **115**, 97-102
19 J. Roth, M. Bendayan and L. Orci, *J. Histochem. Cytochem.*, 1978, **26**, 1074-1081
20 M. Horisberger, M. Vonlanthen and J. Rosset, *Arch. Microbiol.*, 1978, **119**, 107-111

The Development of Gold Drugs

Three reviews have appeared in recent years, which indicate that the development of gold drugs for use in medicine may be entering a new and less empirical phase. They are the following: 'The Biological Chemistry of Gold: a Metallodrug and Heavy-Atom Label with Variable Valency' by P. J. Sadler of Birbeck College, University of London, (*Struct. Bonding*, 1976, **29**, 171-214); 'The Mammalian Biochemistry of Gold: an Inorganic Perspective of Chrysotherapy', by C. F. Shaw III of the University of Wisconsin-Milwaukee, (*Inorg. Perspect. Biol. Med.*, 1979, **2**, 287-355) and 'The Chemistry of the Gold Drugs Used in the Treatment of Rheumatoid Arthritis', by D. H. Brown and W. E. Smith of the University of Strathclyde, (*Chem. Soc. Rev.*, 1980, **9**, (2), 217-240).

Although gold is absorbed by some plants, it cannot normally be detected in animal tissues and is not regarded as an essential element in living systems. Its administration is therefore akin to that of toxic elements such as mercury and basically different from that of biologically used elements such as copper and iron.

Gold distributes widely in the body in which it undergoes a variety of reactions. The most important of these appear to be with thiols, and it undoubtedly exercises some of its biological effects through such reactions and the disturbance which they cause to normal metabolism. New knowledge and new techniques are making studies of these reactions more effective. As is emphasized by Brown and Smith, however, gold is not applied in the form of one drug only and the *in vivo* reactions of compounds such as triethylphosphinegold chloride, Auranofin and sodium aurothiomalate are likely to be quite different. They do not appear to produce a common metabolite on administration and their clearance rates from particular tissues vary, as well as their effects on enzymes. This makes the study of the fundamentals of gold therapy particularly difficult.

Nevertheless, the fact that gold complexes are effective against such a widespread disease as rheumatoid arthritis, for which there is no acknowledged cure, makes their further study important. Although applications of these complexes have been increasing in recent years, their use is still restricted by the toxic effects which are often associated with their administration. There is no reason to believe, however, that their toxic and therapeutic effects are necessarily linked and that research will not lead to more effective complexes and/or to improved conditions of administration. W.S.R.